



Residents' Case Series

A 16-Year-Old Female Presenting With Coma and Hypertension

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A 16-year-old Vietnamese female was admitted to the hospital with new onset generalized tonic-clonic seizures and loss of consciousness. She was in her usual state of good health until the day prior to admission when she developed an acute severe occipital headache. The following night, she was found having generalized tonic-clonic seizure activity for three minutes. After she arrived in the emergency room, she had two further episodes of seizures which were terminated with diazepam. She was started on valproic acid intravenously and was intubated for airway protection. Hypertension required treatment with repetitive doses of intravenous labetalol.

The patient had no significant past medical history as she had no known illnesses and had never been hospitalized. Her past medical history was also unremarkable for surgeries, medications, and allergies. She was a high school student living with her parents and never smoked, drank alcohol, or used illicit drugs. Her father had hypertension and diabetes mellitus, but the family history was negative for any seizure disorders or congenital neurological disease.

Physical examination revealed a well developed female, who was comatose. She was intubated and supported on mechanical ventilation. She was afebrile, had a blood pressure of 200/110 mmHg, a heart rate of 120 beats per minute, and a respiratory rate of 14 breaths per minute by controlled ventilation. The skin showed no neurocutaneous stigmata, the heart was regular in rate, without murmurs, and the peripheral pulses were strong bilaterally. The neurological exam revealed a comatose patient withdrawing to painful stimuli and moving all extremities. The pupils were equal at 3mm and sluggish to direct light, the dolls eyes and corneal reflex was absent and there was no reaction to cold caloric testing. No posturing was noted. Reflexes were equal bilaterally 2+ and the Babinski reflex was present bilaterally.

Laboratory evaluation revealed a sodium of 136 mEq/L (135-145), potassium 3.2 mEq/L (3.5-4.5), Chloride 98 mEq/L (95-105), Bicarbonate 25 mEq/L (22-32), creatinine 0.5 mg/dl (0.6-1.4), and BUN 12 mg/dl (8-18). The CBC revealed a leucocyte count of $16.9 \times 10^9/L$ with no left shift, a hemoglobin of 11.1 g/dL, and platelet count and coagulation studies were within normal limits. Drug screening and serum alcohol level were negative.

She immediately underwent CT scanning of her head which revealed a faint amount of blood within the right Sylvian fissure,

consistent with a subarachnoid hemorrhage. A lumbar puncture was performed which revealed a slightly blood tinged cerebrospinal fluid with an opening pressure of 235 mm CSF fluid. The CSF cell count revealed a significant RBC count of 3820/ μ l (<1) and a WBC count of 3/ μ l (0-10). Glucose level in the CSF was 70 mg/dL (40-80) and total protein in the CSF was 27 mg/dL (15-45). Subsequently, she underwent cerebral angiography which demonstrated mild vasospasm of the branches of the right middle cerebral artery, but no aneurysm or arterio-venous malformation. She was transferred to the ICU, where she received supportive care and standard treatment for subarachnoid hemorrhage, including nimodipine and labetalol.

After a few hours she regained consciousness and became awake, alert, and cooperative. She was extubated on the day of admission. She slowly recovered from the postictal state with a residual right sided nystagmus on left gaze which resolved within three days. She remained hypertensive despite regular dosing of an oral beta blocking agent with occasional symptomatic blood pressure peaks of 220/110 mmHg. Further evaluation consisted of an MRI and MRA of the head which confirmed the small subarachnoid hemorrhage and the absence of an aneurysm. No stenotic lesions of the carotid or basilar arteries were seen and no residual vasospasm was noted. However, the MRI revealed evidence of hypertensive encephalopathy. Although the EKG fulfilled the Sokolow-Lyon voltage criteria for left-ventricular hypertrophy, an obtained echocardiogram showed a normal left ventricular wall thickness.

Workup for secondary hypertension was initiated. A 24 hour urine collection revealed normal metanephrine and urine vanillylmandelic acid levels. The renin plasma activity was elevated with a value of 35 ng/ml/hr (0.2-1.6). Aldosterone was 19.8 ng/L (10-160) while ANA, ANCA and RA factor were within normal limits. A radionuclide renal scan with captopril was performed. The scan showed a regular glomerular filtration rate (GFR) at 97.6 cc/minute (128.8 cc/minute/1.73 m²) and a moderately diminished GFR after application of captopril at 57.2 cc/minute (75.5 cc/minute/1.73 m²). A split-function analysis showed a right GFR of 45.7 and a left GFR of 11.5, suggesting left renal artery stenosis and a normal right renal function.

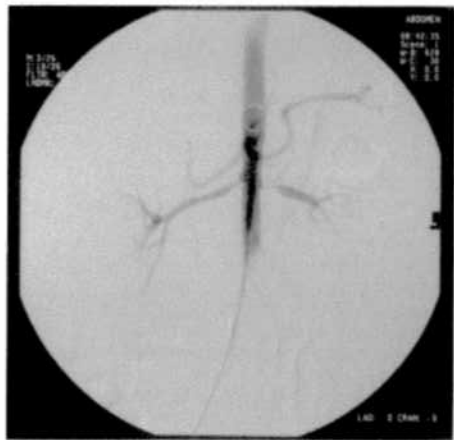
Consequently, a renal artery angiogram with standby balloon angioplasty was performed showing severe bilateral stenosis of the proximal renal arteries (figure 1). This was thought to be due to fibromuscular dysplasia. A bilateral balloon angioplasty was performed, resulting in unsatisfactory angiographic results with persistently elevated trans-stenotic pressure gradients in both renal arteries; thus, endoluminal stents were deployed resulting in satisfactory flow rates with residual trans-stenotic pressure gradients of 3 mmHg and 5 mmHg, respectively.

Anti-hypertensive treatment with metoprolol was stopped the evening before the procedure. Post-procedural systolic blood pressures were ranging between 120 to 135 mmHg and diastolic blood pressures were 62 to 80 mmHg. The patient had no further seizure activity and was discharged one day after the percutaneous revascularization procedure in stable condition and taking one aspirin daily. Follow up after hospital discharge revealed no further seizures, headaches or hypertension.

Discussion

The patient's initial presentation with sudden onset of severe head-

Figure 1.— Digital Subtraction Angiogram of the Renal Arteries, Showing Bilateral Stenosis, Involving The Os.



ache, followed by new seizure activity and loss of consciousness, was highly suggestive of a subarachnoid bleed, which was confirmed by the initial CT scan of the head. Since no ruptured aneurysm or arteriovenous malformations as the cause of bleeding had been identified, other etiologies for the clinical presentation needed to be considered. Although subarachnoid hemorrhage is not typically seen as a complication of hypertension, the MRI was consistent with hypertensive encephalopathy.

Essential hypertension is uncommon in a 16 year old patient. In this setting, a work-up was initiated to identify causes of secondary hypertension, including hyperaldosteronism, pheochromocytoma, or renal artery stenosis. Renovascular hypertension accounts for only 1-2 percent of hypertension in the general population but is the most common cause of secondary hypertension. Certain features can be suggestive of renal artery stenosis, including hypokalemia, absence of family history, duration of hypertension less than one year, and the onset of hypertension before the age of 50 years.

In the general population, there are two different primary diseases causing renal artery stenosis. First, atherosclerotic renal artery stenosis, which typically accounts for about 90 percent of cases, and second, fibromuscular dysplasia, which tends to affect females between 15 and 50 years of age.¹ Fibromuscular dysplasia is considered to be the underlying etiology in the present case. In children, the spectrum of causes for hypertension associated with renovascular disease is different. Given the overall prevalence of this disease, there are only a few published articles addressing this situation. The largest series includes 54 children with hypertension secondary to renovascular disease.² Fibromuscular dysplasia was the most often underlying abnormality accounting for almost half of the cases, followed by neurofibromatosis (15%) and arteritic illnesses (9%).

The evaluation of a patient with suspected renal artery stenosis may, besides the standard tests such as serum creatinine or urine analysis, include more sophisticated, non-invasive studies. This includes functional tests, such as measurement of plasma renin activity, the captopril test, and captopril renal scintigraphy, as well as imaging studies, including duplex ultrasonography, magnetic resonance angiography (MRA), and computed tomography angiography (CTA).

Figure 2.— Digital Subtraction Aortogram of the Aortic Arch, Showing Disease-Free Branches Without Stenotic Lesions, Including the Carotid Arteries.



Initial tests, including serum creatinine and creatinine clearance, were normal. The captopril renal scintigraphy was consistent with left renal artery stenosis. In addition, the twenty times greater than normal renin plasma activity was consistent with this presumed diagnosis. This finding is compatible with an acute stage of renal arterial constriction,³ which later was confirmed by angiography of the renal arteries. A recently published meta-analysis suggests that CTA and gadolinium-enhanced MRA have better diagnostic accuracy than ultrasonography, captopril renal scintigraphy, and the captopril test.⁴

Fibromuscular dysplasia is a non-atherosclerotic and non-inflammatory vascular disease that primarily affects the medium and small-sized arteries, especially the renal and carotid arteries.⁵ In a significant number of patients, more than one vessel is affected. Thus, in this case, concomitant fibromuscular disease of the carotid artery needed to be ruled out by an aorto- and angiogram of the aortic arch branches (figure 2). Depending on the vessels involved, clinical manifestations range from renovascular hypertension to stroke, subarachnoid hemorrhage, abdominal angina, or claudication. The underlying etiology is unknown, despite several hypotheses having been proposed, including those involving humoral and mechanical factors, genetic predisposition, smoking, and conditions causing ischemia of the vessel wall.^{1,5} Fibromuscular dysplasia is further sub-classified by the layer of the arterial wall primarily involved in the disease, namely intimal, medial, or periarterial fibrodysplasia. Of these subclasses, 90 percent involve the medial layer. This subtype presents with the typical "string-of-beads", aneurysmal angiographic appearance. If fibromuscular dysplasia involves the renal artery, the middle and distal segments of the renal artery are usually affected. However, in the subgroup of pediatric patients with fibromuscular dysplasia involving the renal arteries, the vast major-

ity is of the intimal, untypical medial, or periarterial fibrodysplastic type. These types are characterised by lack of the typical series of stenosis and intervening aneurysms, as usually seen in adults (figure 1).⁶ Additionally, fibrodysplastic lesions in children or adolescent are most commonly ostial stenosis, as seen in this case. Even though fibromuscular dysplasia is a histologic diagnosis, it is mostly diagnosed in adults by the clinical presentation and the typical "string-of-beads" stenoses seen angiographically. In contrast, these angiographic features are usually not seen in children; thus, other causes of renal artery stenosis need to be taken in consideration since arteriosclerotic lesions are uncommon in this age group.

The differential diagnosis of fibromuscular dysplasia includes Takayasu's arteritis, and vascular lesions of neurofibromatosis. Similarly, Ehler-Danlos syndrome can angiographically mimic an aneurysmal type of fibromuscular dysplasia. However, Takayasu's arteritis may be the foremost consideration in the differential diagnosis of fibromuscular dysplasia. It is a vasculitis involving large- and medium-sized vessels affecting mostly women below the age of 40. This vasculitis is common in southern and eastern Asia. The aorta is almost always involved as well as the immediate branches of the aortic arch. There are rare reports regarding involvement of the renal arteries in Takayasu's arteritis, which affects the main and the intrarenal branches of the renal arteries.⁷

This patient does not fulfil the criteria for Takayasu's disease and the angiographic appearance does not support this diagnosis, either, since the branches of the aortic arch are free of stenotic lesions (figure 2). Finally, the patient had no stigmata on examination suggestive for Neurofibromatosis or Ehler-Danlos syndrome.

The natural history of renal artery stenosis caused by fibromuscular dysplasia is relatively benign. In contrast to atherosclerotic renal artery stenosis, patients with fibromuscular dysplasia rarely have impaired kidney function. It has been reported that renovascular disease tends to progress in about one third of patients with atherosclerosis, but in only 16% of those with fibromuscular dysplasia.⁵

Treatment options for renal artery stenosis consist of percutaneous or surgical revascularization or medical treatment. The preferred treatment is revascularization in fibrodysplastic renal artery stenosis. It has been shown that regardless of the type of revascularization, 60% of hypertensive patients with fibromuscular dysplasia are cured after revascularization.¹ Thus, percutaneous revascularization with conventional balloon angioplasty is the treatment of choice for patients with uncontrolled hypertension and fibromuscular dysplasia. The procedure has success rates of 82 to 100 percent.⁸

Re-stenosis occurs in only 10 to 11 percent. This is remarkable, considering the re-stenosis rate in atherosclerotic renal artery stenosis is up to 47 percent¹ and in non-stent PTCA procedures of the coronaries at least 42 percent.⁹

In general, conventional balloon angioplasty of the renal artery is sufficient for treatment of the stenotic lesion in fibromuscular dysplasia. Stent placement, as in this case, might be a sufficient procedure if the immediate post-dilatation result by balloon alone is suboptimal.¹⁰ However, long-term results for balloon angioplasty with consecutive stent deployment in fibrodysplastic renal arteries are not available yet. Thus, the rate of re-stenosis remains uncertain. Given the young age of the patient, the stent was placed understanding that the patient may need bypass surgery in the future.

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